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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/925,796	08/09/2001	Casey C. Case	8325-0007.01	5123

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EXAMINER
BRUSCA, JOHN S

ART UNIT	PAPER NUMBER
1631	7

DATE MAILED: 08/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/925,796	CASE ET AL.	
	Examiner	Art Unit	
	John S. Brusca	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5,6,8-33 and 87-113* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5, 6, 8-33 and 87-113* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 August 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The papers received on 17 June comprising an Information Disclosure Statement (paper 5) have not been made part of the permanent records of the United States Patent and Trademark Office (Office) for this application (37 CFR 1.52(a)) because of damage from the United States Postal Service irradiation process. The above-identified papers, however, were not so damaged as to preclude the USPTO from making a legible copy of such papers. Therefore, the Office has made a copy of these papers, substituted them for the originals in the file, and stamped that copy:

COPY OF PAPERS

ORIGINALLY FILED

If applicant wants to review the accuracy of the Office's copy of such papers, applicant may either inspect the application (37 CFR 1.14(d)) or may request a copy of the Office's records of such papers (*i.e.*, a copy of the copy made by the Office) from the Office of Public Records for the fee specified in 37 CFR 1.19(b)(4). Please do **not** call the Technology Center's Customer Service Center to inquiry about the completeness or accuracy of Office's copy of the above-identified papers, as the Technology Center's Customer Service Center will **not** be able to provide this service.

If applicant does not consider the Office's copy of such papers to be accurate, applicant must

provide a copy of the above-identified papers (except for any U.S. or foreign patent documents submitted with the above-identified papers) with a statement that such copy is a complete and accurate copy of the originally submitted documents. If applicant provides such a copy of the above-identified papers and statement within **THREE MONTHS** of the mail date of this Office action, the Office will add the original mailroom date and use the copy provided by applicant as the permanent Office record of the above-identified papers in place of the copy made by the Office. Otherwise, the Office's copy will be used as the permanent Office record of the above-identified papers (*i.e.*, the Office will use the copy of the above-identified papers made by the Office for examination and all other purposes). This three-month period is not extendable.

Specification

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR §§ 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR §§ 1.821-1.825 for the following reasons:

Several nucleotide sequences appear in the specification on pages 54-57 that are not properly identified. Nucleotide sequences must be identified by sequence identification number. Furthermore, if said sequences do not appear in the sequence listing, a new listing including said sequences must be supplied. It is often convenient to identify sequences in figures by amending the Brief Description of the Drawings section (see MPEP 2422.02). If said sequences consist of a portion of sequences already of record in the sequence listing, they may be identified in the specification using the existing SEQ ID No. accompanied by the position of the sequence on the already listed sequence.

Applicants are required to comply with all the requirements of 37 CFR §§ 1.821-1.825. Any response to this Office Action which fails to meet all of these requirements will be considered non-responsive. The nature of the sequences disclosed in the instant application has allowed an examination on the merits, the results of which are communicated below.

Inventorship

3. The request to correct the inventorship of this nonprovisional application under 37 CFR 1.48(a) is deficient because:

The application file contains the required statement of the assignee under 3.73(b) and a substitute Rule 63 Declaration adding F.Urnov as an inventor. However. perhaps through Office error, the application file does not contain a request for the change of inventorship or a statement of the person being added to the inventorship. It is noted that fees have been charged for such a petition in the instant application. Upon filing of the missing papers, the request for a change in inventorship will be approved.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 2, 5, 6, 8-20, 24-28, 30, and 87-113 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of delivery of zinc finger proteins to cells by introduction of an expression vector, does not reasonably provide enablement for methods of delivery of zinc finger proteins to cells by introduction of exogenous zinc finger

proteins to cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In In re Wands (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation." These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to practice the claimed invention one of skill in the art must regulate endogenous gene expression by delivery of a zinc finger protein to a cell. For the reasons discussed below, there would be an unpredictable amount of experimentation required to practice the claimed invention.

b) The specification does not give specific guidance to deliver zinc finger proteins to cells and cause modulation of expression of an endogenous gene.

c) The specification does not provide working examples of delivery of zinc finger proteins to cells to cause modulation of expression of an endogenous gene.

d) The nature of the invention, regulation of gene expression by zinc finger proteins, is complex.

e) A search of the prior art does not show regulation of gene expression by delivery of zinc finger proteins to cells by any direct method. Beerli et al. (reference AD-1 in the Form PTO

1449 filed 17 June 2002) and Liu et al. (reference AG-1 in the Form PTO-1449 filed 17 June 2002 show that the teaching of the prior art at around the effective filing date of the instant application used exclusively expression vectors to introduce engineered zinc finger proteins into cells.

f) The skill of those in the art of molecular biology is high.

g) The prior art does not address the predictability of the full scope of the claimed invention.

h) The claims are broad in that they read on embodiments that are not supported by the instant specification or the prior art.

In order to practice the claimed invention, the skilled practitioner would first turn to the teachings of the instant specification to practice embodiments of the claimed invention in which zinc finger proteins are delivered as protein to cells. However, the instant specification does not provide specific guidance or working examples of such embodiments. As such, the skilled practitioner would turn to the prior art for such guidance, however the prior art also does not provide such guidance. Finally, said practitioner would turn to trial and error experimentation to practice the full scope of the claimed invention without guidance from the specification or the prior art. Such represents undue experimentation.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 22, 23, 26, 28, 29, 32, and 33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 22, 23, 29, 32, and 33 are indefinite for recitation of the phrase in line 2 of claim 22 "a second zinc finger protein-encoding nucleic acid" because it is not clear if the zinc finger is the second zinc finger of claim 1. The rejection would be overcome by amending claim 22 to recite "a promoter operably linked to a nucleic acid that encodes the second zinc finger protein."

Claim 26 is indefinite because it is not clear whether step (v) includes administration of a nucleic acid encoding the second zinc finger protein. The rejection would be overcome by amending claim 26 to explicitly state the step (v) further comprises administration of the nucleic acid encoding both the first and second zinc finger proteins.

Claim 28 is indefinite because it is not clear if the exogenous agent induces expression of an expression vector encoding zinc finger proteins or if the exogenous agent is an expression vector encoding the zinc finger proteins. The rejection would be overcome by stating that the exogenous agent induces expression of the zinc finger proteins encoded by an expression vector.

For the purpose of examination, the claims have been assumed to incorporate the suggested amendments.

Double Patenting

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would be obvious over, the reference claim(s). see, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

9. Claims 1, 2, 8-12, 14-16, 87, 90, 92-94, 96, 97, 102, 104, 106 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 9, 11, 13, 14, 18-22, 23, and 26 of copending Application No. 09/942090. Although the conflicting claims are not identical, they are not patentably distinct from each other because it would be obvious to use genes not operably linked to heterologous sequences because such species of the copending generic claims are disclosed in paragraph 51 of copending Application No. 09/942090. It would be further obvious to use a negative control of a zinc finger

that binds to a second gene because such controls are disclosed as useful in the method of the copending generic claims in paragraph 38 of copending Application No. 09/942090.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

10. Claims 1, 2, 5, 6, 8-33, 87, 88, and 90 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3, 5, 8-10, 12-22, 26, 27, 32, 39-41, and 55 of U.S. Patent No. 6,599,692. Although the conflicting claims are not identical, they are not patentably distinct from each other because it would be obvious to use a negative control of a zinc finger that binds to a second gene because such controls are disclosed as useful in the method of the issued generic claims in columns 4, 7, 10, and 36 of U.S. Patent No. 6,599,692.

11. Claims 1, 9, 10-12, 14-16, 87, and 92 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim4, 9, 11, and 13-22 of copending Application No. 09/941450. Although the conflicting claims are not identical, they are not patentably distinct from each other because it would be obvious to use genes not operably linked to heterologous sequences because such species of the copending generic claims are disclosed in page 17 of the corresponding U.S. Patent Application Publication No. US 2002/0164575 A1 of copending Application No. 09/942090. It would be further obvious to use a negative control of a zinc finger that binds to a second gene because such controls are disclosed as useful in the method of the copending generic claims in page 17 of the corresponding U.S. Patent Application Publication No. US 2002/0164575 A1 of copending Application No. 09/942090.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca whose telephone number is 703 308-4231. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 703 308-4025. The fax phone numbers for the organization where this application or proceeding is assigned are 703 872-9306 for regular communications and 703 872-9306 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308-0196.

John S. Brusca
Primary Examiner
Art Unit 1631

jsb
August 9, 2003